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Development and Validation of a Clinically Usable Prediction Model for Other-Cause Mortality in Men with Prostate Cancer using Two Prospective National Cohorts

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Purpose/Objectives

Other-cause mortality (OCM) is the primary cause of death in men with localized prostate cancer. Competing risks of OCM can often render prostate cancer treatment or treatment intensification futile. However, few tools exist to predict OCM in this population. Those that have been developed are often too complex for routine clinical use, or lack robust validation. We therefore aimed to develop a clinically usable, validated prediction model for OCM in men with prostate cancer using two prospective national cohorts to help personalize treatment decision making.

Materials/Methods

Model training was performed using the National Health and Nutrition Examination Survey (NHANES), a cross-sectional, nationally representative survey conducted every two years in the United States. We included men ages $\geq$ 40 from 1999-2008, with mortality follow-up through 2014. After selecting a list of predictors that could be readily obtained in clinic, we built three candidate models with all-cause mortality as the outcome using Cox proportional hazards or random survival forest modeling. The models were validated in the Prostate, Lung, Colon, and Ovarian (PLCO) Cancer Screening Trial with OCM as the outcome. Model performance was evaluated using time-dependent area under the curve (AUC).

Results

The NHANES training data included 1,887 men with 613 deaths during follow-up. Median age was 60 years. Sixty-eight percent of patients had at least one non-prostate cancer comorbidity (previous myocardial infarction, emphysema, chronic bronchitis, diabetes, hypertension, previous stroke, liver comorbidity, arthritis), 32% had a BMI $\geq$ 40, and 22% were current smokers. The PLCO validation data included 8,146 men over

age 55 diagnosed with prostate cancer, of whom 2,389 died of other causes. Median age was 69 years, 60% had at least one non-prostate cancer comorbidity, less than 1% of patients had a BMI greater than 40, and 9% were current smokers. The Cox model had the best performance in the training and validation cohorts. In the training cohort, it had a time-dependent AUC of 0.86 and 0.87 at 10 and 14 years, and in the validation cohort it had a time-dependent AUC of 0.74 and 0.76 at 10 and 14 years. The final model included 8 predictors: age, education level, marital status, diabetes, hypertension, stroke, BMI, and smoking status.

Conclusions

We have developed and validated an OCM model that can readily be used in clinic and specifically in men with prostate cancer. Our OCM prediction model uses only 8 easily obtained predictors and shows comparable or superior performance to more complex OCM prediction models already in existence, some of which include over 100 variables. An online application will be made available to produce instantaneous OCM predictions from our model to help guide clinical decision making.

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